Changes in chlamydia prevalence over time: how to observe the unobserved

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The ways that widespread testing and treatment of sexually transmitted *Chlamydia trachomatis* infections affect the prevalence and incidence of infection at the population level are not easy to understand, and the difficulties are well documented.[1] First, chlamydia is an infection, so the dynamics of transmission between infectious and susceptible individuals are given by a non-linear function. Second, chlamydia screening recommendations were introduced without randomised controlled trial evidence of the effects of screening on prevalence. Third, most chlamydia infections are asymptomatic, so no reliable signal in surveillance data exists that distinguishes between changes in incidence and testing. Fourth, yearly population-based prevalence surveys with adequate coverage and precision are financially unfeasible.

To help interpret the real-world effects of widespread chlamydia testing, England has more comprehensive and complete surveillance data[2] than most countries. And, by chance rather than design, the British National Surveys of Sexual Attitudes and Lifestyles (Natsal) measured *C trachomatis* prevalence in 1999–2001 (Natsal-2; just before the National Chlamydia Screening Programme in England, [NCSP] started its roll out) and 2010–12 (Natsal-3; just after the NCSP achieved countrywide coverage).[3] The essence of the dilemma is that point prevalence estimates in the two surveys were nearly identical—chlamydia prevalence in women aged 18–24 years was 3·1% (95% CI 1·8–5·2) in Natsal-2 and 3·2% (2·2–4·6) in Natsal-3—and CIs were compatible with a decrease or increase in prevalence. But complex transmission dynamic mathematical modelling studies had predicted that, with the levels of investment and test coverage that the NCSP achieved, chlamydia prevalence should have dropped measurably and sustainably by now.[4]

In a model-based analysis, Joanna Lewis and Peter White[5] aim to clarify what might have happened between, and since, Natsal-2 and Natsal-3. The advantages of their approach are that they use national data on chlamydia testing and diagnosis and they developed a mathematical model that represents the relationships between uninfected and infected groups of people, with a minimal level of complexity. The code for the model is available online, so anyone can reproduce the findings and explore the model further.

The model does not make predictions but allows a post-hoc interpretation of what might have resulted in the inferred changes in prevalence year by year. Lewis and White[5] propose that increasing chlamydia test coverage in the NCSP to more than 20% of men and more than 40% of women by 2010 resulted in a reduction in chlamydia prevalence, which occurred between the Natsal-2 and Natsal-3 data collection periods. The model-estimated rebound in prevalence, from 2011 to 2012, coincided with a decrease in chlamydia testing.

The model probably does not include some essential processes. Sex differences in prevalence and incidence highlight important issues. Between 2000 and 2007, prevalence inferred by the model increased in men and decreased in women (based on the authors' preferred estimates of testing). The data presentation, as year-to-year changes, can be difficult to interpret. Using the

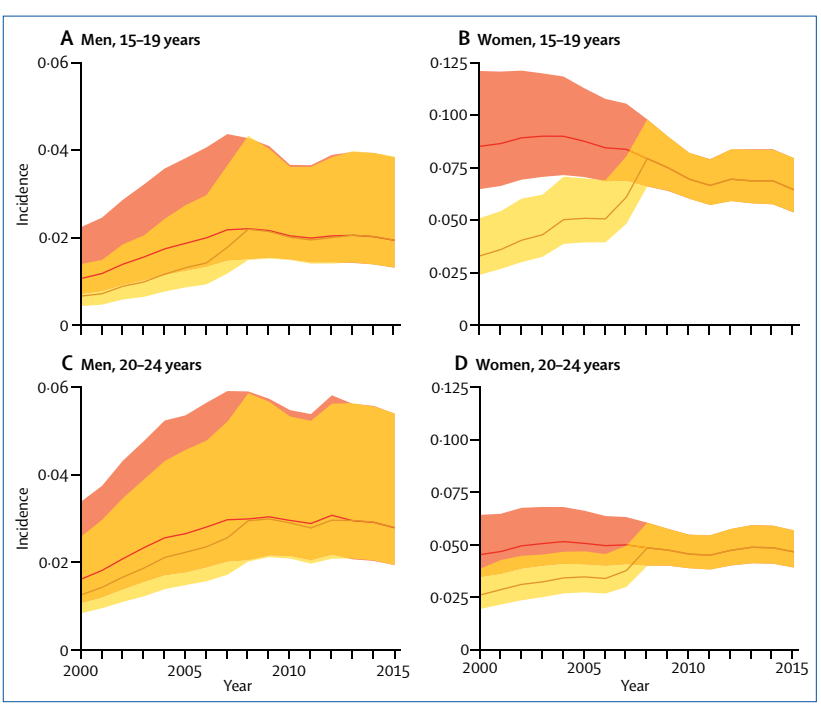

Figure: **Model-estimated *Chlamydia trachomatis* incidence rates, 2000–15**
Data are estimated from the model published by Lewis and White.[5] Lines show median estimates and shading shows 95% credible intervals. Red shows estimates using maximum numbers and orange shows estimates using minimum numbers.

published code to plot absolute chlamydia incidence rates, with the maximum testing and diagnosis estimates, the model output estimates that between 2000 and 2007, chlamydia incidence rates increased by a factor of 2·04 (95% credible interval 1·92–2·14) in men aged 15–19 years and by a factor of 1·84 (1·76–1·91) in men aged 20–24 years (figure 1). Lewis and White[5] suggest that male sexual risk-taking behaviour increased during that period, but this explanation is not entirely convincing because the substantial changes that would be needed to result in such large changes in incidence should affect both men and women. Data from Natsal[6] and from the USA over the same period,[7] did not find marked or sex-specific changes in behaviour.

Increased test coverage but poorer targeting over time of people with chlamydia could also explain a negligible decrease in prevalence. The model assumes the same screening rate in uninfected and infected people, although people at higher risk of chlamydia infection are more likely to be tested.[3,8,9] NCSP test coverage targets after full implementation resulted in more tests, but the diagnosis rate did not change, suggesting that tests were done disproportionately amongst uninfected people.[10] Thus, the model outputs are consistent with Natsal-2 and Natsal-3 prevalence estimates but, to balance the increase in screening rates, the model estimates large increases in incidence in men and high absolute incidence in women.

At the public health level, the model output suggests that large increases in chlamydia testing were compatible with a modest temporary reduction in chlamydia prevalence, well below expectations. Whether these changes represent good value for money can be debated.[4] Duration of infection might, as Lewis and White suggest, be a better indicator of programme performance than prevalence. However, adopting this measure depends on the reliability of model-estimated prevalence and incidence.

Lewis and White's study[5] highlights important research priorities. Empirical estimates of *C trachomatis* incidence in the presence of widespread testing would be very valuable. Further mathematical modelling studies should investigate reasons for the gap between model-predicted and observed reductions in chlamydia prevalence, including the effects of differential testing according to infection status. And, a fourth Natsal is needed to provide the next estimates of *C trachomatis* prevalence and of sexual behaviour in Britain. National chlamydia control strategies need to be informed by sound evidence of effectiveness and optimal chlamydia case management. The search for robust indicators to monitor the dynamics of *C trachomatis* during screening interventions continues.

Nicola Low, Joost H Smid
Institute of Social and Preventive Medicine, University of Bern, 3012 Bern, Switzerland
nicola.low@ispm.unibe.ch

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